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FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/583,738	GHANBARI ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *23 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *23-33,35-47 and 49-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *51-58* is/are allowed.

6)☐ Claim(s) *23-30,33,35-44 and 47-50* is/are rejected.

7)☐ Claim(s) *24,27,28,31-33,38 and 45-47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 51-58 are allowed.

Claims 23-33, 35-47, 49-50 and 51-58 are pending.

Rejections Withdrawn

Prior art rejections over Merril et al (US Pat. 5,688,501) and Merril et al in view of an additional reference are herein withdrawn in light of new grounds of rejection.

Rejections Maintained

1. Claims 23-25, 33, 37-39 and 47 rejected under 35 U.S.C. 102(b) as being anticipated by Norris (US Pat. 4,957,686) , for reasons of record in paper number 18.

Allowable Subject Matter

2. Claims 31-32 and 45-46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

3. Claims 51-58 define over the prior art of record and therefore define allowable subject matter.

Response to Arguments

***Please Note*:** In so far as Applicant's arguments apply to the new grounds of rejection set forth below, Merrill (US Pat. 5,688,501) will be addressed.

is traversed on the grounds that:

a. Merril does not teach virulent bacteriophage having a broad host range; and

b. Merril does not teach a virulent bacteriophage preparation comprising two or more bacteriophage strains.

2. It is the position of the examiner that (see Paper #18, paragraphs 11, 13, 15 and 17, incorporated herein by reference) that Merril utilizes bacteriophages that are genus specific (see Merill claim 13) that would be effective against a plurality of species and stains of bacteria. Each genus of bacteria is made of up of a plurality of species, and each species is made up of a plurality of strains.. The compositions of Merrill et al are taught to be genus specific, and effective against "bacterial species and strains (see col. 7, lines 34-35). Therefore virulent bacteriophages that have a broad host range are disclosed by Merril, albeit described using different terminology, the compositions disclosed and utilized in the claimed methods are the same or equivalent bacteriophages as now claimed, as the bacteriophages of Merril are effective in eliminating bacteria in a method of treating infection (see Merril claim 1-16).

With respect to preparations of two or more bacteriophage strains, it is the position of the examiner that Merril clearly suggests and teaches combinations of two or more bacteriophage strains through teaching the following;

"The present invention is not limited to a specific bacteriophage or a specific bacteria. Rather, the present invention can be utilized to develop anti-HDS modified bacteriophages which can be used to treat any and all infections caused by their host bacteria." Merril goes on to teach "it is particularly contemplated that the methods described herein will be very useful as a therapy (adjunctive or stand alone) in infections caused by drug-resistant bacteria" and lists a plurality of bacteria, and there corresponding bacteriophages for production of adjunctive compositions. Adjunctive compositions would contain a combination of therapeutic that comprise two or more species and strains of bacteriophage directed against drug resistant bacteria (see Merril, col. 7, lines 17-36). The term used by Merril to teach the combination of two or more bacteriophages is

the word "adjunctive". The examiner found the definition of the word "**adjunctive**" mean joining; forming an adjunct (http://poets.notredame.ac.jp/cgi-in/wn?cmd=wn&word=adjunctive))

"**adjunct** 1. Something attached or added to something else but not an essential part of i.

Thesaurus: supplement, complement, addition, accessory, extension, auxiliary (http://www.allwords.com/query.php?SearchType=3&Keyword=Adjunct)).

Therefore, Merril et al inherently discloses compositions that comprise two or more bacteriophages added together in the treatment of drug-resistant bacteria (see col. 7, lines 26-67 and col. 8, lines 1-41).

3. The rejection of claims 23-25, 33, 37-39 and 47 rejected under 35 U.S.C. 102(b) as being anticipated by Norris (US Pat. 4,957,686) is traversed on the grounds that Norris does not teach bacteriophage capable of infecting more than one strain of S.sanguis.

4. It is the position of the examiner that while Norris does teach that each bacteriophage is specific for one kind of bacteria, this does not preclude the bacteriophage from effectively killing more than one strain of the same bacteria, or two strains from different species or genera of bacteria. A strain can be second type of the same bacteria, a different species of the same genus The process steps recited in claim 23 require the bacteriophage preparation to comprise:

(1) two or more bacteriophages (see Norris, col. 4, claim 3; col. 3, lines 46-53) streptococci (see Streptococcus mutans and Streptococcus sanguis col. 3, line 1 and lines 50-52; col. 4, line 43), staphylococci (see Staphylococcus aureus, col. 4, line 19);

(2) the bacteriophage are isolated against different strains of bacterial organisms (see Norris cited support under paragraph (1) immediately above);

(3) each bacteriophage strain is effective in killing (see Norris , col. 3, line 38 "destroy" the host bacteria);

(4) the preparation can be safely administered to patients or mammals (see Norris, col. 3, lines 46-53; patient in need of preventing dental carries); together with a pharmaceutically acceptable carrier , such as a tablet, liquid, dental floss, tooth cleaning powder, gum, and mouth wash solutions(see Norris, col. 3, lines 54-57; col. 4, claims 4-10).

New Grounds of Rejection

Claim Objections

5. Claim 24 is objected to because of the following informalities: Claim 24 recites the phrase "bacterial organism" in the singular tense and depends from claim 23 which recites the phrase "bacterial organisms" in the plural tense; the difference in noun tense introduces a lack of clarity into the claim. Appropriate correction is required.

6. Claim 27 is objected to because of the following informalities: Claim 27 recites the term "fruendii"; this should be –freundii--. Appropriate correction is required.

7. Claim 28 and 42 are objected to because of the following informalities: Claims 28 and 42 depend from claims 24 and 38 respectively, and recite the phrase "Klebsiella oxytoca"; this phrase lacks antecedent basis in claims 24 and 42, which recites "Klebsiella pneumoniae". Appropriate correction is required.

8. Claims 33(f) and 47(f) are objected to because of the following informalities: The claims recite the phrase "resistant to resistant to"; the second recitation of the phrase "resistant to" is redundant. Appropriate correction is required.

9. Claim 38 is objected to because of the following informalities: Claim 38 recites the phrase "bacterial organisms" and depends from amended claim 37 which recites the phrase "bacterial infection (preamble)"; the phrase "bacterial organisms" lacks antecedent basis in claim 37 from which it depends. Appropriate correction is required.

Claim Rejections - 35 USC § 102

10. Claims 23-24,27, 29, 33, 37-38, 41,43, 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Unilever (EP 0414304A2).

Unilever discloses the instantly claimed invention directed to a method of treating infection (see col. 4, lines 3-5) in humans or animals (see col. 1, lines 10-12), the method comprising the step of:

administering a composition that comprises a bacteriophage preparation (see col. 2, lines 18-23) that contains at least two bacteriophage strains (see claims 3-13 for species of composition) that are able to kill (lysis and bacterium destroyed, see col. 2, line 29-31) propionibacterium acnes(see claim 7), together with other bacteria ; see claims 9-13), Streptococcus mutans, Bacteroides gingivalis and Haemophilus actinomycetemcomitans (see claim 12) and have a broad host range (see col. 2, lines 53-55).

Additional embodiments include bacteriophages against Staphylococcus epidermdis (see col. 7, line 2), E.coli, Proteus mirabilis, Vibrio flurvalis, Citrobacter freundii, Enterobacter agglomerans, E.vulneris, Pseudomonas fluorescens, Actinomyces viscosus and Streptococcus sanguis (see col. 6, lines 42-43), wherein the reference discloses the administration of compositions that comprise more than one bacteriophage

(see abstract), for the treatment of infection (therapy, col. 7, claim 13) caused by undesirable microorganisms (see abstract, and entire document). The composition comprises a pharmaceutically acceptable carrier (see col. 3, lines 54-58, cream, lotion, oil, emulsifier, water; toothpaste or mouth was (see col. 4, lines 14-24) and phage compatible additives (see col. 4, lines 25-29).

The phage composition was resistant to drying (see col. 5, line 8), and free of bacterial cellular debris, specifically catabolic enzymes (see col. 4, lines 46-48), and therefore would be not toxic to the mammal/animal. Inherently the reference anticipates the instantly claimed invention.

11. Claims 23-24,27, 29, 33, 37-38, 41,43, 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Day et al (EP 0403292, 1990).

Day et al disclose the instantly claimed invention directed to a method of treating infection (see abstract) in mammals (see claims), the method comprising the step of:

administering a composition that comprises a bacteriophage preparation (that contains at least two bacteriophage strains (see page 3, lines 53-56; see claims 7-10) that are able to kill the disease causing bacteria, wherein the composition contains bacteriophages directed against two different pathogens, specifically Streptococcus equines and Enterococcus durans (see Example 2, page 5), together with a pharmaceutically acceptable carrier (see page 4, lines 9-34; Example 1, page 5, dextrose).

The bacteriophages were resistant to drying (see page 5, Example 1, paragraphs a) and c)). Inherently the reference anticipates the instantly claimed invention.

12. Claims 23,35, 37, 49 are rejected under 35 U.S.C. 102(a) as being anticipated by Golosova et al (SU827064 B, 1981).

Golosova et al disclose a method of treating bacterial infection through the administration of a composition that comprises bacteriophages specific for at least two bacterial strains, specifically bacillus proteus, bacillus pyocyaneus and staphylococcus (line 4 of abstract and title). The method also comprises the administration of antibiotics and a corrective micro flora preparation, of bifidum bacteria or coli-bacterin (see English abstract, first line and last two lines). The reference inherently anticipates the instantly claimed invention.

Claim Rejections - 35 USC § 103

13. Claims 23-30, 33, 35-44, 47, 49-50 are rejected under 35 U.S.C. 103(a) (new grounds of rejection,) as being obvious over Day et al(GB 2253859, 1992) in view of Merrill (US Pat. 5,688,501)

Day et al (GB 2253859) teaches bacteriophage compositions that comprise "at least two strains of phage specific for one host (see page 5, paragraph 5), as well as combination compositions that comprises bacteriophages directed against more than one bacterial pathogen (see page 6, paragraph 4) for the purpose of administering effective bacteriophage therapy to a mammal in order to over come natural protective mechanisms of bacteria, wherein "bacteria are known to be able to develop resistance to phage infection (see page 5, paragraph 5)" and the incorporation of at least two bacteriophages against two or more strains of bacteria, would provide effective means for "elimination of the unwanted organism (see page 6, paragraph 1)"

even if the microorganism develops a resistance to one phage or one phage becomes lysogenic (see page 6, paragraph 1).

Day et al differ from the instantly claimed invention by failing to show the combination at least two bacteriophages together with an antibiotic, and bacteriophages for additional species of bacterial pathogens.

Merril et al teach the administration of compositions that comprise bacteriophages together with antibiotics (see col. 9, lines 11-63) and/or chemotherapy, delivered together with a carrier, excipient, vehicle, and can be in lyophilized form (see cols 9-10), and teach a plurality of bacteriophages that are effective in the elimination of a plurality of pathogenic bacteria (lytic at the genus level) to treat any and all bacterial infections in an analogous art for the purpose of carrying out an effective method of treating bacterial infection with compositions that comprise bacteriophages together with antibiotics.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to administer a composition that comprises two or more bacteriophage strains isolated by the method of Day et al directed against different strains of bacteria taught by Merril et al because Merril et al teaches the importance of treating bacterial infectious diseases (see Merril et al, col. 3, lines 45-51), for the realized effective "in vivo killing of bacterial pathogens (see Merril et al, col. 4, lines 48-49)" "across the spectrum of bacterial diseases (see Merril et al, col. 6, lines 63-68), wherein the two or more bacteriophages would be effective to kill (Day et al), "all the clinically important members of the family Enterobacteriaceae (see Merril et al, col. 7, lines 37-39), which includes two or more species and strains of clinically

important Salmonella (see Merril et al, col. 7, lines 57-67; col. 8,lines 1-2), Escherichia (see Merril et al, col. 7, lines 40-49) and additional pathogens (see Merril et al, col. 7-8).

The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of treating a bacterial infection with a composition that comprises two or more bacteriophages against two strains of bacteria in combination with the antibiotic of Merril et al, because Merril et al teach and suggest adjunctive therapy to treat infections would provide for the combination effect in a method of treating bacterial infection(see Merril et al, col. 9, lines 1-9). In the absence of a showing of unexpected results, Day et al in view of Merrill et al obviate the instantly claimed invention.

Conclusion

14. This is a non-final action.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

16. Evdokimenko et al (RU1533330C, English abstract) disclose a method for prevention and treatment of bacterial infection, specifically coli-bacteriosis, wherein the method comprises the step of administering a composition of a mixture of at least two bacteriophages, which has higher activity, wider action spectrum, and higher specificity than previous preparations, and comprises a pharmaceutically acceptable carrier, distilled water.

17. Williams et al (1983, abstract) is cited to show several compositions of two bacteriophage against various strains of E.coli (different serotype strains).

18. WO90/03122 (1990) are cited to show bacteriophage preparations specific for three Clostridium species, and two lactic acid bacteria for the treatment of infection (see pages 21, paragraph 1, page 19 and page 13).

19. WO95/27043 is cited to show methods of treating infections caused by antibiotic resistant bacteria.

20. SU1790380 (1993) is cited to show bacteriophage preparations for Streptococcus bovis for the treatment of infection and to increase milk production (see abstract in English).

21. Ru2036232 and Su172960 are cited to show compositions that comprise preparations of mixtures of bacteriophages directed against a plurality of strains, species and/or genera (see English abstracts).

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703) 308-7543. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703)308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

Vgp
November 25, 2003

LS
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600